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AN EXPERIMENTAL AND THEORETICAL INVESTIGATION
INTO THE PUPILLARY SYSTEM FOR RESPONSE TO LIGHT

FRANK H. BAKER

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An Experimental and Theoretical Investigation into
the Pupillary System for Response to Light

By

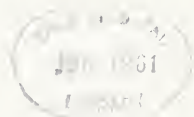
Frank Howard Baker, A.B.

Harvard, 1956

A thesis submitted to the faculty of the Yale University
School of Medicine in partial fulfillment of requirements
for the degree of Doctor of Medicine.

Section of Neurology
Department of Internal Medicine
Yale University School of Medicine

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The conception and completion of this work can only be attributed to the author's contact with numerous men in biology and engineering who, with insight and stimulation, have led this author to the foundation on which was built the necessary correlations. Such indebtedness is particularly due to Dr. Lawrence Stark, under whom this work was done, and his co-workers.

This thesis is submitted to the faculty through Dr. Gilbert Glasser of the Department of Neurology.

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CHAPTER I

PREFACE

This work attempts a broad analysis of the form of pupillary response to light and the mechanisms which combine to determine this response. The literature is voluminous, though quantitative data had to await the development of suitable pupilometers in more recent times. Many studies have been extensive in both the experimental and theoretical realms. It is surprising, in fact, the amount of interest in this system which has captured the minds of scientists throughout the ages. Modern times has seen some very fine and extensive experimental investigations as well as some well worked out theoretical formulations. This work will combine these two approaches.

The pupil system possesses certain properties which make it attractive for a study of neural reflex and control.

- 1) The end organs are superficial and readily available without the need for dissection.
- 2) Though the retina is acknowledged to be a highly elaborate structure, the small number of central synapses make this relatively uncomplicated as a CNS system.
- 3) Although secondary factors such as fatigue and alertness of the subject influence pupillary activity, the fact that learning apparently does not occur simplifies analysis of data and experimental design using human subjects.

- 4) As opposed to many other reflexes this has a readily defined teleological foundation.

Thus, the system is simple, functionally complete and readily manipulatable, and as has been mentioned, investigators have not neglected these virtues.

We will precede, then, with a review of some of the pertinent anatomy and physiology and present some new experimental work. Using concepts from systems analysis, we will then investigate theories of system operation under certain circumstances and draw some broad conclusions.

CHAPTER II

ANATOMY OF THE SYSTEM.

Parasympathetic system:

The pupillary light reflex encloses an arc from retina through midbrain to pupil. Retinal afferents probably perform the dual role of conveying visual information and carrying light intensity information for the pupil response (Schweitzer, 1956). Optic nerve fibers send off collaterals which project to the region of the rostral portion of the third nerve nucleus (Ranson and Magoun, 1933). Many investigators feel that there is a single synapse in the pretectal region, though Polyak (1957) presents evidence that the pregeniculate nucleus, anatomically closely associated with the main geniculate nucleus, acts as a way station for the pupillary tract and sends axons to the oculomotor nucleus by way of the pretectal region without synapse. In any event, there is agreement that there is decussation of the pathways from the two geniculate bodies prior to synapse on motor ganglion cells. The parasympathetic final common pathway therefore receives contra and ipsilateral innervation at this point, and the consensual reflex is established. Pupil activity on the two sides is highly correlated. Cells in the rostral part of the third nerve nucleus, generally thought to be located primarily in the well delineated Edinger-Westphal nucleus, send preganglionic parasympathetic motor fibers to the ciliary ganglion by way of the third nerve. After a synapse in

that structure, the reflex pathway is completed through the short ciliary nerves which pierce the sclera at the posterior pole of the globe and travel to the sphincter pupilli.

Sympathetic system:

Without doubt the sympathetic nervous system plays a part in determining level of operation and dynamic behavior of the pupil under certain conditions, as has been substantially shown by Lowenfeld (1958). She has brought together evidence indicating the presence of a psychosensory center in the hypothalamus, and she has placed on a firm foundation the presence of a discrete radial dilatory muscle. The outflow of the sympathetic system proceeds mainly through the first two thoracic segments up the chain to synapse in the superior cervical ganglion. Postganglionic fibers travel into the cranium on the carotid, leaving the artery before its termination to seek a path crossing the floor of the middle ear and thence to join the third nerve distal to the gasserian ganglion. Long ciliary nerves carry the signal to the globe partly bypassing and partly through the ciliary ganglion without synapse.

CHAPTER III

REVIEW OF THE PHYSIOLOGY

Pupillary noise:

Under average lighting conditions and fixed accommodation, one notices a persistent fluctuation in the size of the pupil not obviously correlated with other physiological activity. Stark, Campbell and Atwood (1958) have pointed out that there is high correlation between the fluctuation of the two pupils. Noise power increases with retinal illumination. The spectra of the noise signal and pupil response have different break frequencies with parallel attenuation and therefore require partially separate channels. Conclusions as to where the noise could be injected into the system and the nature of the source were reviewed. Lowerstein (1950) has shown much decreased noise activity after lesions in the hypothalamic center of pupil sympathetic activity in monkeys, implicating the sympathetic as the more probable pathway.

Pupil threshold:

Work on pupil threshold to increases of light intensity has been reviewed by Schweitzer (1956), who also contributed experimental evidence carried out with an infra red optical system, determining threshold activity by subjective methods. For small simulating fields pupil threshold was found to be much below visual threshold, but as the field was enlarged sensitivity of the pupil system increased and with large fields approximated visual thresholds.

Therefore, unlike the visual system, spatial summation is a fundamental property of the pupil system. As to temporal summation, though, the two systems act similarly. Within a specific, small interval, measured by Bouman (1950) to be 0.02 and 0.035 secs. cases threshold depends on total energy independent of time distribution, (the Bunsen-Roscoe Law). As the time distribution of energy increases beyond that critical value threshold energy values increase. These two insights into threshold dependence on time and area parameters, reveals the fact that constant energy stimuli yield constant responses, given certain bounding limits of stimulus duration and space variables. Threshold experiments have also revealed that the pupillary reflex is not dependent on one class of receptor (Schweitzer, *ibid*; Lowenstein and Lowenfeld, 1959), though Lowenstein notes that the red, as opposed to the white light gives the larger, more sustained response.

Response to static input:

When light is suddenly applied to the dark adapted eye and then maintained constant for a period of time, there results an initial sharp constriction which may be maintained in a plateau for several seconds, subsequently followed by a slow dilation over a period of minutes to some relatively fixed area, less than the dark adapted area. There is great variability in the data among various investigators of the static response (reviewed by Schweitzer), but in general plots of pupil area vs. wide field illumination result in

sigmoid shaped curves. (Reeves, 1918). The teleological effect of such a pattern of response is to allow effective functioning over a very broad operating range.

Dynamic response - steps and impulses:

Talbot (1939) used a large field for stimulation and recorded pupil diameter photographically. He described a response to a step input of light which began after a latency of 0.25 secs., occasionally preceded by a small dilation, showed a "jog", or rapid change of rate of contraction after 0.6 secs. with decreased velocity, and a second jog at 0.9 secs. The transient was completed in 2.5 secs. For small responses, less than a 1.5 mm. change, the peak was followed by an immediate, relatively rapid dilation or rebound. Latency of the dilatory phase following step decrease of light was 0.4 secs. at an initial speed of 0.25 mm/sec., half the rate of initial constriction. The response to an impulse of light showed the latency, speed, and the characteristic discontinuities seen in the step response. Of particular note was the observation that the minimum duration of the transient was 1.1 secs. For short flashes (up to 1 sec. duration), he found that the amplitude of the response varied with the stimulus energy, but that there was a falling off of response at higher intensities. In an elaborate theoretical discussion he postulated an interplay of the two muscles, radial and constrictor, which had mechanical properties of tension and elasticity. A proper coordination of excitation times would then give rise to the characteristic

jogs, which played an important part in his scheme. He also assumed that the frequency of nerve impulses was proportional to log intensity with rapid formation of chemical muscle excitant and therein derived an exponential formula for contraction with a time constant dependent on step intensity.

Van der Tweel (1959) was also interested in developing a model of the pupil system based on experimental data of the overall response to steps and impulses and assumptions about the behavior of the system elements inferred from other general physiological work. His experimental method used an optical system in which the pupil was illuminated by deep blue light and the image of diameter was projected onto moving blue sensitive film, thus giving a continuous record of pupil diameter. Unfortunately the resolution of the technique was poor, but his data is somewhat similar to Talbot's and ours on points of comparison. His data seemed to indicate that the peak of responses to impulse stimuli with durations up to 0.5 sec. had a constant time duration to peak, and he thought that within this time range the stimulus appeared to be a trigger mechanism, the height of the response being related to the initial flux by a log function. A second flash applied 0.3 - 0.5 secs. after the first showed summation logarithmically. Also, he reasoned from the fact that since time constants of contraction to both large and small stimuli was constant, the motor element could not be amplitude limited in the range he investigated. Unlike Talbot and Lowenstein (see below), in considering dilation, van der Tweel assumed that

dilation was passive, based mainly on the fact that his data demonstrated that the speed of dilation depended on the peak diameter reached following an impulse. He noted that dilation approximately followed an exponential curve.

Lowenstein and co-workers have done much work on phases of the pupil over a period of many years using cats, rodents, birds and primates; and neurophysiological techniques of injury ablation and pharmacological devices. His instrumentation has included infra-red photography and, recently, an infra-red scanner which selects the pupil diameter from a sampling of pupil segments made ten times a second. He has studied the form of the response with a view to the fine points of the pattern and has given much weight to the first derivative of the response curve as an indicator of fundamental physiological processes. The light reflex in his conception is finely balanced between sympathetic and parasympathetic control (Lowenstein and Lowenfeld, 1950); interference in this balance produces characteristic changes in reflex pattern. In the normal pupil contraction is in a single wave of acceleration and deceleration to a peak occurring several tenths of a second after the cessation of the one second stimulus impulse. Redilation is achieved in two phases. The first is fast and is primarily parasympathetic inhibition. The second is slower and requires an intact sympathetic connection for its completion. Peripheral sympathectomy has an effect on the contraction phase, viz. 1) latency of contraction is shorter; 2) amount of contraction is greater; 3) speed of contraction is greater; and 4) time to peak is shorter. An interesting change in the response

occurred after hypothalamic lesions in monkeys. The rate of contraction was increased, but constriction halted abruptly before the end of the one second stimulus. The pupil maintained contraction on a plateau until 0.1 or 0.2 tenths seconds after the end of the stimulus, and then redilation took place rapidly. Lowenstein and Lowenfeld (1952) have correlated changes in the response with fatigue with responses after CNS lesions and have thereby formulated an hypothesis of the temporal development of fatigue: central structures fatigue before peripheral elements and the sympathetic system before parasympathetic. Psychosensory events such as a loud noise will restore the failing reflex.

Dynamic response - sinusoidal input:

Stark and Sherman (1957) initiated a study which has become the most thorough investigation of the sinusoidal response of the pupil. They reasoned that since the pupil controlled retinal flux which was in turn a factor in pupil response, the dynamic operation of the system should most properly be studied with the aid of servo-analysis, the science of feedback control systems.

A review of the properties of a servomechanism is in order here. An arch-typical servosystem is the thermostatically controlled heating system of a house in which a device samples room temperature and operates a second device which adjusts room heat so that the activation of the sampling device is minimal. This may be represented schematically as shown in Fig. 1. The boxes represent elements in

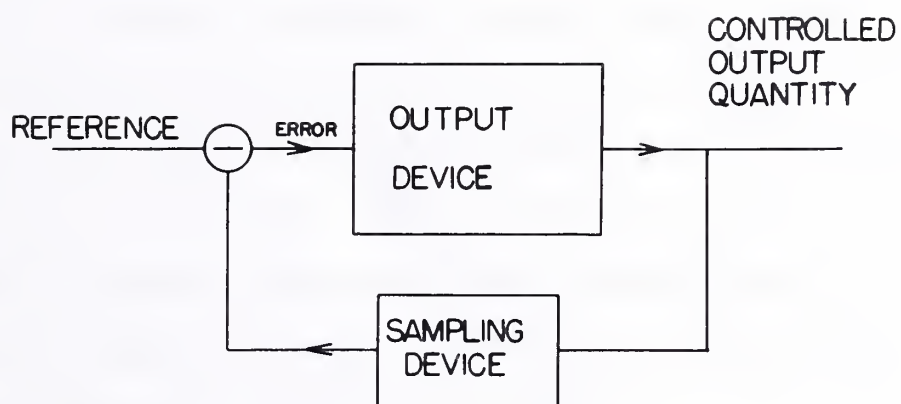


Fig. 1. Simple servomechanism. Output quantity compared with desired reference value and difference used to drive output device. Arrows designate unidirectional signal flow.

the system and the connecting lines with arrows denotes the path of the signal, or information. The left hand junction of the three line segments at the circle enclosing the minus sign represents a subtraction operation taking place between the reference value and the sampled value of the controlled quantity. Therefore, in our representative control system, temperature is the output quantity. The thermostat samples the temperature of the room and compares the resulting value with a predetermined desired value, the reference. If an error results, the output device is activated to adjust the temperature to a new value by putting in or removing heat. In recent years the theory of such devices has been worked out to a high degree for the linear case (for example, Bower and Schultheiss, 1958; and Chestnut and Mayer, 1951). Important properties are speed of response, minimization of error, and stability.

In applying servothory to the pupil system, Stark and Sherman were confronted with the problem of describing the control process which was taking place at the plane of the pupil. If a broad source projects a given intensity of light onto the whole eye, the flux which falls onto the pupil will be

$$F = AxI$$

in obvious symbolism. Any change in F may be described by a change in A or a change in I . Therefore, in difference notation:

$$\Delta F = Ix\Delta A = Ax\Delta I$$

If

$$\Delta F_i = Ax\Delta I$$

and

$$\Delta F_o = Ix\Delta A$$

then

$$\Delta F = \Delta F_i + \Delta F_o .$$

A step change of light due to a change in I would travel around the control loop and cause a change in A. The above notation allows us to calculate the gain as

$$G = \frac{\Delta F_o}{\Delta F_i} = \frac{I_x \Delta A}{A_x \Delta I}$$

This formulation has the difficulty that one is forced to choose what will be the intensity I to be used in calculating the numerator, i.e., the I before the change, or after the change. Those authors worked mainly with sinusoidal inputs which varied about a mean $\bar{I}$. If the peak to peak change (ΔI) could be kept small, the error introduced by this complication would be negligible.

The initial work, then, described the properties of the open loop system response. The data indicated an amplitude response break frequency at 1.5 cps and a nonminimum phase shift which suggested asymptotic limiting at -270° . Justifying a linear system on their small signal approximation, they deduced from servothory a model system which had three lags and a gain of 0.16. Their phase data gave a transport delay of 0.18 secs., and after postulating equal time constants for all lags, arrived at the open loop transfer function

$$G(S) = \frac{0.16e^{-0.18S}}{(1+0.1S)^3}$$

This is merely the Laplace transform of the system's response to sinusoidal inputs. The transform contains all the necessary parameters for completely describing the behavior of a linear system, and therefore by proper manipulation will give the differential equations of response in time (Stark, 1959).

Stark and Baker (1958), using arguments from servothory and employing drugs to shift system parameters explained the origin of the previously described "induced hippus", the 1.4 cps occillation of the pupil seen under special lighting conditions.

Tyler, working in this laboratory, critically reviewed the problem of representing the pupil system by a linear lumped parameter network. Working with his own data on sinusoidal and step on and off response, he concluded that there was no real asymptote in the phase-frequency curve and had difficulty correlating frequency response with step response data. Such conceptual complications led him to construct a model on feed-forward lines. Though his objections were aptly presented, his discussion was along highly theoretical lines and without real physiological basis.

CHAPTER IV

PRESENT APPROACH

From the foregoing discussion we have seen that there are several factors which determine the area of the pupil:

- 1) Intensity of light falling on the retina,
- 2) area of retina illuminated,
- 3) past and present time course of the light intensity at the retina,
- 4) state of adaptation of the retina,
- 5) distribution of the light flux between the two retinas,
- 6) internal random influence on pupil area, or noise.

As we have seen from Schweitzer's work, 1) and 2) may be combined as

$$F = A' \times I'$$

where I' = intensity of light at the plane of the retina and A' = the area of retina illuminated. We will not consider the effect of binocular imbalance, point 5), which is too complicated for this preliminary study and may be controlled by standardizing experimental conditions. In point 6) we recognize the fact that other influences than light level have a part in the determination of pupil area. Accommodation is one of these forces and may be controlled experimentally; fatigue and psychosensory phenomenon can be controlled less well; and we are finally left with "noise", the random uncorrelated variations in pupil area and a subject for study in itself. Finally,

since the state of retinal adaptation is a function of the time course of incident flux, we see that pupil area at any moment in a controlled situation is ideally determined only by the past and present course of incident flux, or symbolically:

$$A = f(F)$$

The fundamental problem:

The simplicity of the foregoing conclusion draws us to the brink of the total problem of the physiology of the pupillary reflex to light, almost by a process of reduction ad absurdum, namely: how can we determine the response to light at any time given any previous light flux history? The answer to such a question would presumably lead through all the ramifications of submicroscopic structure and function. It is to the delineation of the nature of the problems raised in a search for a general theory that we are devoted here.

An apology:

The central reason for the rise of mathematics in any science is no better stated than by Philip E. B. Jourdain (1956):

"Our ideal in natural science is to build up a working model of the universe of the sort of ideas that all people carry about with them everywhere 'in their heads,' as we say, and to which idea we appeal when we try to teach mathematics. These ideas are those of number, order, the numerical measures of times and distances, and so on."

In short, even if a mathematical construct adds nothing new to our concepts, such a representation is valuable for its clarity, economy, generality, and systemization, for it is in such an atmosphere that correlations, the reasons for science, are made.

Biology has, to a great extent, resisted the inroads mathematics has made into the physical sciences. Much of the tardiness has undoubtedly been due to the complexity of the material and its refractoriness to experimental control, but as Margeneau says (1950):

"Talk about the complexity of organisms, about the sum that is more than its parts, usually winding up in the reminder that biology is a field for which casual analysis is inadequate, proves nothing. Aristotelian physicists have said the same thing about inorganic nature. Indeed every field of human interest in which significant variables (variables of state) have not been discovered is for that very reason complex and intractable, and to say that it defies casual analysis is merely to admit that it has thus far not been penetrated by the usual methods of science."

In studying the pupillary reflex to light we are dealing with a system which is acted upon by a forcing variable, light, and reacts in a characteristic response mediated by a system of transferences and transformations of information. Solutions to the problems presented by such a study parallel in many ways methods in systems analysis and the science of response of physical systems. Indeed, Norbert Wiener, who is frequently accused of trying to fabricate brains out of machines, in reality has appealed to the economy of human effort, when he explains the touchstone of his philosophy in the Introduction to Cybernetics:

"There are fields of scientific work, as we shall see in the body of this book, which have been explored from the different sides of pure mathematics, statistics, electrical engineering, and neurophysiology; in which every single notion receives a separate name from each group; and in which important work has been triplicated or quadruplicated; while still other important work is delayed by the unavailability in one field of results that may have already become classical in the next field."

In the course of this study we will therefore not hesitate to draw from these fields for methods of symbolic representation, experimental approach, and formal analysis.

Systems analysis - an introduction.

The case in point is a system made up of real components strung together in some manner, which reacts in a measurable way (the output) to the stress of a forcing function (the input). On p. we used the simple notation of connecting the diagrammatic representation of two measurable points of our real system, viz, input and output, by lines and boxes. The boxes represented the real lumped elements of the system which generate, store, dissipate or transform energy, or information. The lines connecting the boxes represent unidirectional transfer of information unchanged from one element to another. A simple system might therefore be diagrammed as in Fig. 2. where the input function is e_1 , which is transformed into an output e_0 through two operators G_1 and G_2 . By knowing that there exists two distinct system elements we infer, or perhaps have measured, an intermediate quantity e_1 . Obviously, if we knew only the input and output of the system and nothing of its mechanism of operation, we would have

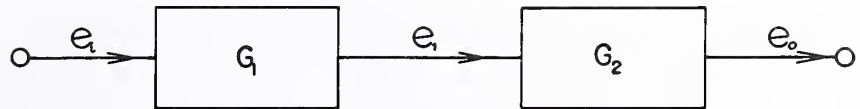


Fig. 2. Two element series network. Signal flow representation of transformation of e_i into e_o by operators G_1 and G_2 .

simply represented the transformation $e_i \rightarrow e_o$ by a single block, G . One can see, then, that this notation, the block diagram, can be expanded as our insight into mechanisms of the system increases.

Concentrating on the first block, we will call the operator G_1 a transfer function. Using the notation of modern algebra, the transformation $e_i \rightarrow e_o$ becomes

$$e_1 = G_1 e_i$$

In general, these functions are not commutable, i.e.

$$e_1 \neq e_i G_1$$

in the general case. This becomes evident on the consideration of nonlinear operators to be discussed shortly. The transformation may also be visualized in the usual manner using the graph of the function.

Finally, since $e_o = G_2 e_1$,

The complete system is represented algebraically as

$$e_o = G_2 G_1 e_i,$$

again noting that in general

$$G_2 G_1 e_i \neq G_1 G_2 e_i.$$

The properties of the operators fall into general classes, two of the most important being linear and nonlinear operators. Since there are well developed methods in linear analysis and nonlinear analysis is still troublesome, difficult or impossible, attempts are

frequently made to approximate the properties of systems by linear functions. The property of linearity is based on the principle of superposition to which a system conforms if the sum of two or more input functions yields an output function equivalent to the sum of outputs to the individual inputs, or

$$\begin{array}{lcl} \text{If} & y_1 = f(x_1) \\ & y_2 = f(x_2) \\ & \vdots \\ & \vdots \\ & \vdots \end{array}$$

$$\text{Then} \quad y_1 + y_2 + \dots = f(x_1 + x_2 + \dots)$$

With such a system if the input is doubled, the output is doubled.

In passing it should be noted that if an operator varies with time, the system may still be linear (see Ku for a discussion).

While for some purposes, particularly when there is a need for mathematical analysis in verification or synthesis, one can throw away much important information when the linear approximation is attempted, in fact a realization of the properties conferred by nonlinear elements can contribute much to an understanding or analytical dissection.

We are now in a position to note the validity of the statement that the operators in the algebraic notation are not commutable in the general case. If, for example G_1 was linear and G_2 generated the log of its argument, then

$$e_1 = G_2 G_1 e_i = \log (ae_i + c)$$

$$\text{and} \quad e_i = G_1 G_2 e_i = a \log e_i + c$$

These are two wholly different functional relationships.

Selin (1958) suggested the use of just such a differential point in the study of a nonlinear property in the pupil system. He

reasoned that, for the purposes of his analysis the pupil system could be broken down into two elements: 1) A frequency dependent element, in which the output for any given amplitude input was dependent on frequency, and 2) an amplitude dependent element which saturated at higher values of input but was independent of frequency. These functions are represented in figures 3 and 4. If the G_2 element precedes the G_1 element, the break point of the system transfer function would be independent of the input, e_i . On the other hand if the frequency dependent component comes first and high, saturating levels of input are being used the output at low frequencies would saturate the nonlinear element while at high frequencies the input to G_2 would be less than the critical value e_c . The comparison of the frequency responses is shown in Fig. 3.

A purely analytic method has been used to 'dissect' the system.

The approach:

The remainder of this work will be an exploration of the ideas of systems analysis in their application to the pupil system.

The experimental problems to be confronted are the determination of the functional relationships governing the response of the pupil under different operating conditions. Explicitly the questions are:

- 1) How does the response to an impulse of light depend on
 - (a) the duration of the input function and (b) the height of the impulse?

2) How does the response to sinusoidal varying light depend on:

(a) the peak to peak variation, and (b) the mean value of the stimulus?

With this data at hand it will be in order to draw some inferences about the operation of the system.

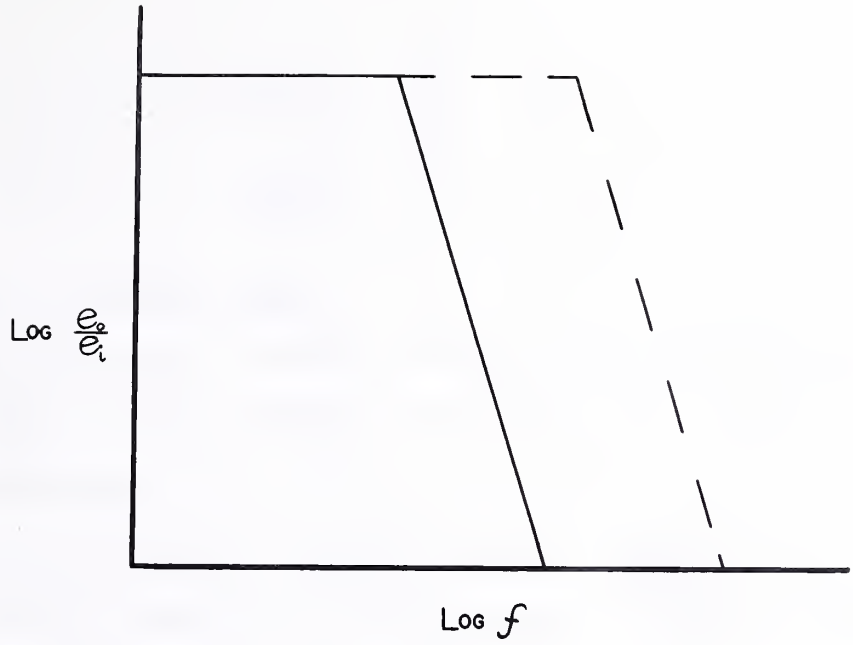


Fig. 3. Diagrammatic frequency response function. Solid curve represents response of frequency dependent operator. Dashed curve represents response of saturating system in which saturating operator follows frequency dependent operator.

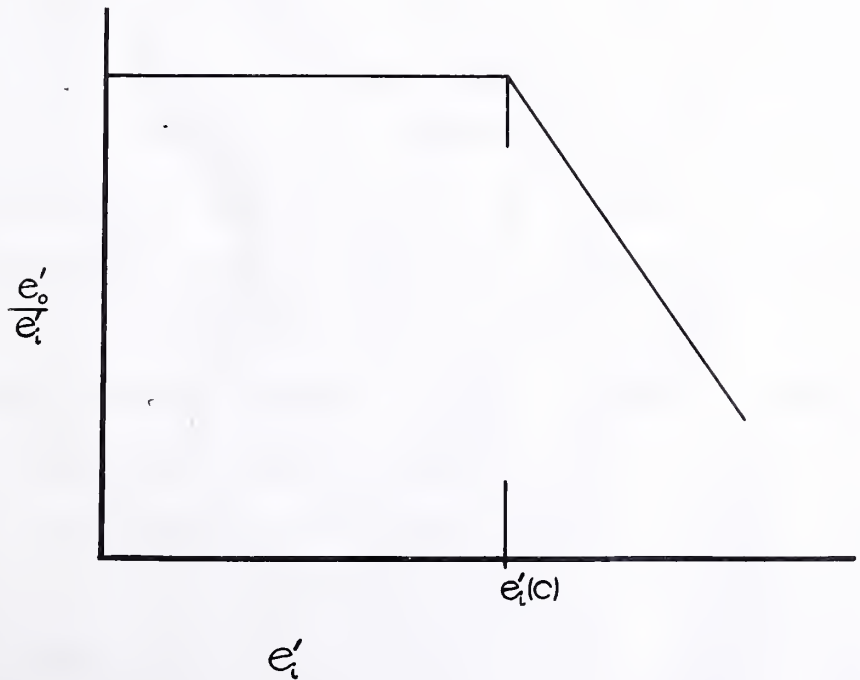


Fig. 4. Input-output relationship of saturating element. Gain independent of input for all values less than $e_i'(c)$.

CHAPTER V

METHODS

Instrumentation - the pupillometer:

The methods used for stimulating and recording pupil area have been reviewed elsewhere (Stark, 1959). They will be discussed here for completeness.

The pupillometer is composed of three subunits, each with a partly independent light path, but all ultimately directed through an objective lens before the eye.

1) The infrared channel:

A beam of light from a high intensity tungsten source passed through an infrared filter and was focused on the iris in a circle always larger than the pupil. The amount of the infrared light reflected from the iridopupillary plane was, to a good approximation, inversely proportional to the pupil area, and the intensity of the reflected component was detected by a properly oriented infrared photocell. The resulting output was recorded on a Sandborn pen recorder simultaneously with a record of the light input. Increases in light level and decreases in pupil area were recorded as positive deflections, whence the terminology "rising" and "falling" phases, etc. The infrared filter in the impulse experiments was composed of two Kodak 87c filters tandem. A faint dark red could be seen by the dark adapted subject when the stimulating light was covered, but this was all but masked by even the absolute minimum intensity of the stimulating light. In the sinusoidal experiments an army snooperscope filter was used and was absolutely opaque to visual wave lengths.

2) Stimulating channel:

A Sylvania glow modulator lamp was used as the stimulating source. It had frequency response characteristics well beyond the pupil range, and because its output could be completely controlled electronically, it was ideally suited for this application. Its one disadvantage was the range of flux variation which was limited by a minimum low level as well as the maximum. Kodak neutral density filters could be inserted into this path to reduce transmittance. The flux from this source was focused at the plane of the pupil as a small circle always smaller than the smallest area of the pupil. In this way change in pupil size would have no effect on the amount of light reaching the retina, and this manner of operation is called "open loop".

3) Calibration channel:

Calibrations used to correlate absolute pupil area with infrared photocell output were obtained photographically along a third light path.

The proper use of this equipment required much cooperation on the part of the subject. Trained laboratory personnel were therefore used in these experiments. They were also able to apply their knowledge of the method towards observations made during the course of the experiment and thus give valuable information on adjustment of the equipment.

Experimental procedure:

1) General precautions:

There is much variability in the response of the pupil from one moment to the next and from run to run. Certain precautions, though, were used to reduce the scatter. The experimental sitting was planned for the morning after a good night's sleep. The subject was dark adapted 4 to 5 minutes to a level of illumination less than the minimum which would be presented. During the experiment room light was well controlled so that only the stimulating light determined operating conditions. After the subject had taken position for an experimental run, he was adapted to the conditions of the run for a period of at least 15 secs. In the case of the impulse experiments, two impulse trials were given at the beginning of the first trial, and the run followed. Between runs the subject rested and dark adapted. The atmosphere was kept quiet to reduce psychosensory phenomenon.

2) Impulse experiments:

A function generator produced rectangular impulses of variable height and width. A neutral density filter with a transmittance of $1/10$ was used in the stimulating path and the maximum stimulating flux was given an arbitrary value of one. Flux varied between 0.1 and 1.0 on an arbitrary scale, and impulse widths varied from 0.01 to 0.4 secs. Longer impulse durations were not used in order that a trial would have as little influence as possible on the light adaptation of succeeding trials.

A trial was a single application of light at some parametric value and recurred in periods of 10 secs. If there were to be five parameter changes, a five by five latin square was formed of these values. A row of this square gave the succession of values to be used in each run. There were three replications at each value forming a group, and changes of values were made during the light-off free intervals. In summary, then, for a five by five square, three trials formed a group at one value; five groups at different values made a run, and the experiment was composed of five runs.

The pen recorder was run at a speed of 25 mm/sec. and gave good resolution of the rising phase of the response. Since the response of the Sandborn recorder could not reproduce the input pulse forms except to indicate the foot of the rise and the crown of the fall, stimulating light output was monitored on an oscilloscope.

In the analysis of the data values were read directly off the recording chart as relative pupil area (area x constant). Values of maximum rate of rise were secured by drawing slopes to the rising phase at the point of maximum rate of change.

3) Sinusoidal experiments:

All experiments were run at a frequency of 1.4 cps. This was chosen as an optimum between the irregularities and distortions seen at the lower frequencies, and the low amplitudes of response found at the higher frequencies. Mean flux values were varied between extremes of transmittance of 1 to 10^{-2} ; percentages of modulation ranged between 0.1 and 0.75. The experiment was designed around a

greco-latin square in which 5 values of each parameter were randomised among 25 runs. Each run was preceded by dark adaptation and was followed by a calibration.

Analysis of the data necessitated subjective selection of good pieces. Particularly at lower frequencies, a gaiting effect suppresses response, then allows a period of response to come through. The criterion for selection was to favor the larger responses of the run, but then only provided that they came in blocks of 2-3 waves and had a phase lag characteristic for that frequency. The relative amplitudes were measured on the recording graph and converted to absolute area units.

Statistical methods:

The inherent biological variability of this system required the use of replication and statistical methods to extract the greatest amount of information from the experiments. Also, change in the internal operating conditions of the system with time had to be relegated to an inferior position in the determination of the dependencies under investigation. Towards these ends use was made of the experimental design technique developed by R. A. Fisher (1951). These techniques are based on the requirement that each parametric value be accorded an equivalent or combined standing within the plan of experimental grouping and coordination. On paper a design will therefore take the form of a square array of rows and columns of the values of the variables. Each value appears once in each column and each row and is assigned its place randomly.

In the case of the sinusoidal experiments a value was two dimensional being composed of percentage modulation and mean light level values. The resulting array is called a greco-latin square. To extract the functional relationship, rows and columns of the array were arranged to give the values for each parametric value, percentage modulation and mean level respectively. These were plotted to give graphical representation to the functional relationships. Such data can also be analyzed for variance and thus a numerical comparison of dependence on the two variables was made. In the case of the impulse experiments each value of the array was one dimensional and thus there was a replication of each value by the order of the array (4x or 5x).

CHAPTER VI

RESULTS

Impulse response:

General form: (See Fig. 5)

The rising phase is characterized by a latency, an accelerating phase, inflection point, decelerating phase, and peak. Following the foot of the stimulus impulse, a 0.25 sec. latency intervenes before the initial rise of the response. The function has a rising phase which reaches a maximum acceleration in about 0.2 secs. and then decelerates to the peak of the response. Times to peak averaged $0.56 \pm .02$ secs., except for responses to the 0.4 sec. impulse which showed 0.1 sec. longer duration. The falling phase, (redilation) again had a significant foot and inflection point. Throughout its course it was much slower than the rising phase. Later segments of the curve showed more variability in the morphology of the response; random behavior became more prominent and the shapes of the curves take on different forms. In general the second phase gradually decelerated in an exponential-like manner shown in Fig. 5. There was a characteristic slow uniform dilation in the later phases which makes curve fitting of the whole curve by simple exponential functions unsuitable. Responses to extremes of the input variables did not show large differences. Fig. 6.

Quantitative data:

Figure 7 demonstrates the variables in which we will be interested and their notation.

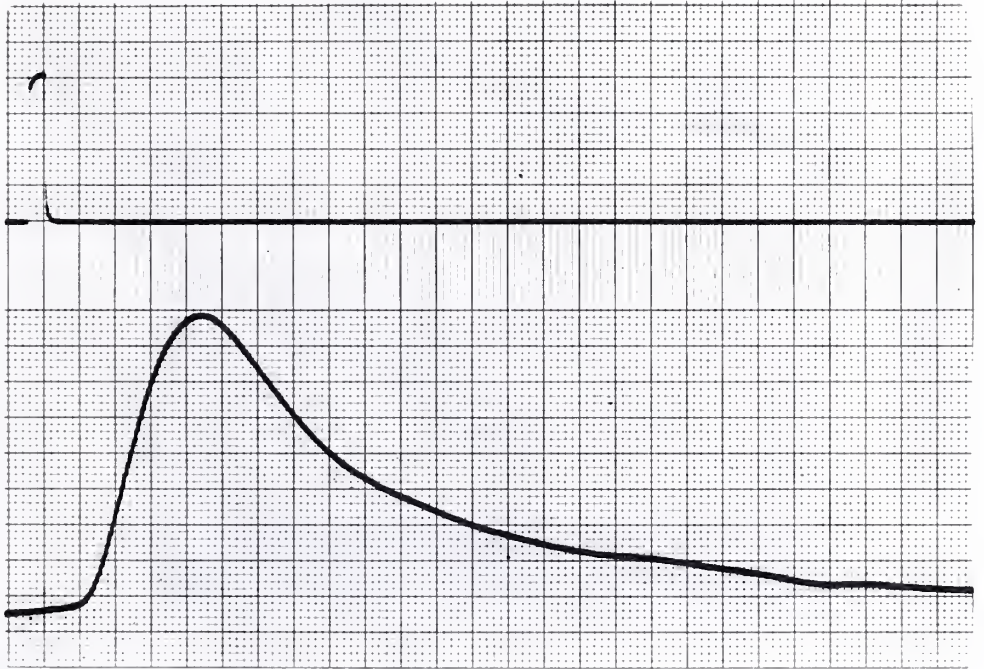
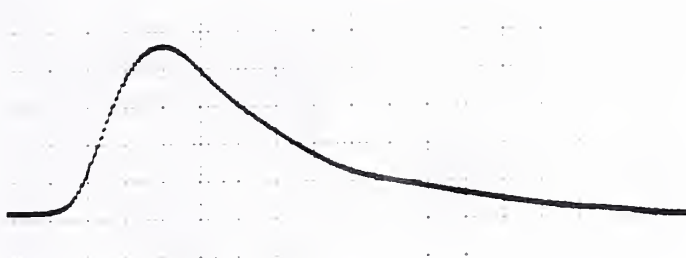
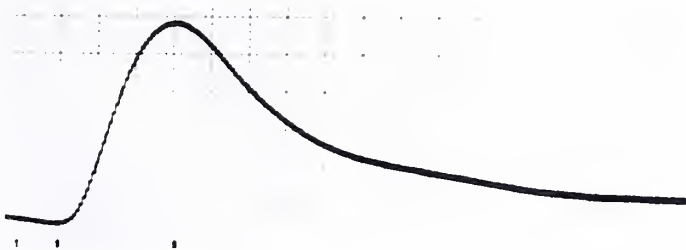


Fig. 5. Representative response to pulse. Pulse duration equals 0.1 sec.; amplitude equals 0.5 units. Abscissa is time axis (each large division equals $1/25$ sec.); ordinate is axis of amplitudes (relative).

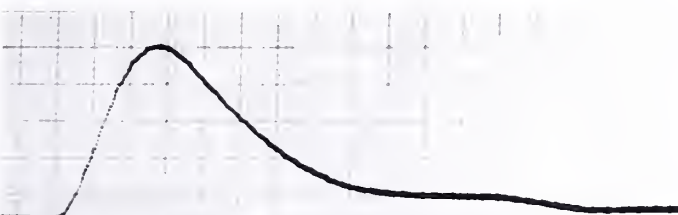
(a)



(b)



(c)



(d)

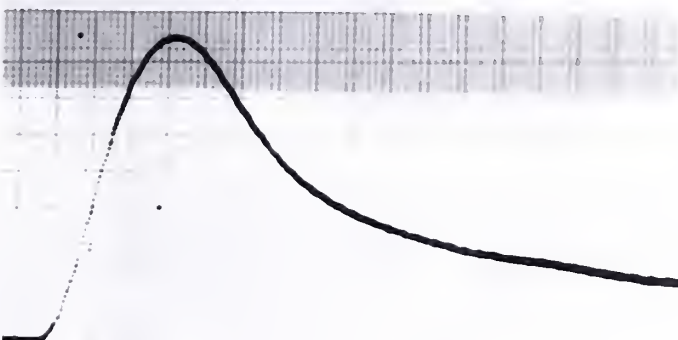


Fig. 6. Responses to extremes of pulse parameters. First two samples illustrate extremes of amplitude (duration constant at 0.05 secs.): impulse amplitudes equal 0.1 in (a) and 1.0 in (b). Last two samples illustrate extremes of duration (amplitude constant at 0.5 units): impulse durations equal 0.1 in (c) and 0.4 in (d).

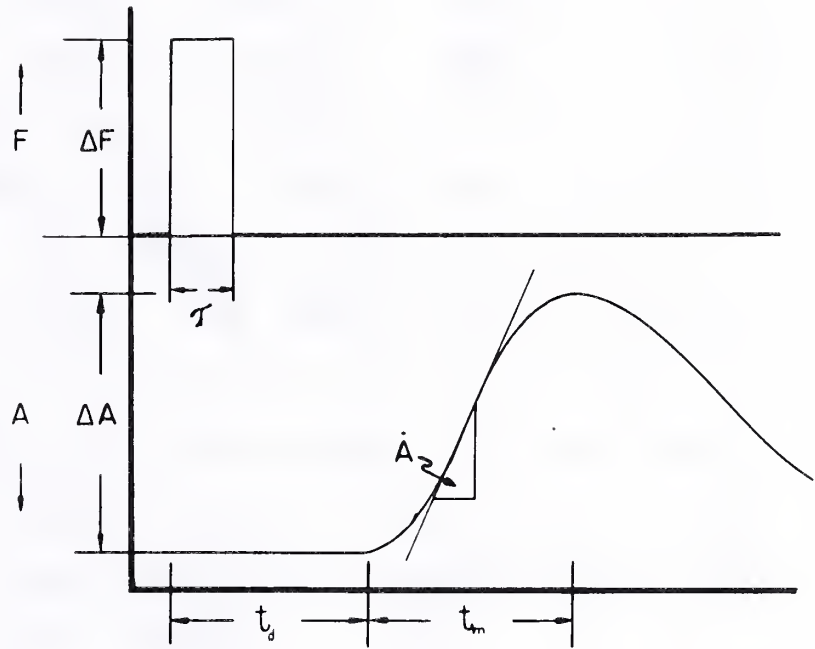


Fig. 7. Impulse parameters with symbolism used in text.

Response height bears a different relationship to impulse duration than to impulse height. Impulses of duration 0.05 or greater show gradual increase of area change with increasing duration. The curve relating response to impulse height characteristically has a small curvature, rising rapidly from low values. Fig. 8 plots results from an experiment varying impulse duration and below, in Fig. 9 is shown results from an experiment varying impulse height. A log plot of this data is shown in Figs. 10 and 11 respectively.

Maximum rate of rise: Changing impulse width had little effect on the maximum rate of rise except at the 0.01 sec. duration value, which was significantly diminished. There was, though, a dependence of maximum rate of change on change in impulse height. Fig. 12 plots rates of change against response height and the relationship proves to be relatively linear.

Results section - "Sinusoidal Experiment"

A selected piece of data from a sinusoidal experiment is illustrated in Fig. 13, and response dependence on variations of input percentage modulation and mean light levels are plotted in Figs. 14 and 15. The former diagram demonstrates a heavy dependence of output and change on percentage modulation. Dependence on mean light level is less significant. This observation is borne out by variance analysis which attributes a variance of 1-3 to variation in percentage modulation, while only 0.3 is due to change in mean light level. Over moderate ranges of operation the output of the pupil system may therefore be said to be relatively independent of mean operating level.

Section 1: Introduction and Purpose of the Study

The purpose of this study is to investigate the effects of the proposed changes on the overall performance of the system. The study is divided into two main parts: a theoretical analysis and an experimental evaluation. The theoretical analysis will focus on the mathematical models and the expected outcomes of the changes. The experimental evaluation will involve the implementation of the changes in a real-world environment and the measurement of the resulting performance metrics. The results of the study will be presented in a series of tables and graphs, which will be used to compare the performance of the system before and after the changes. The study is expected to provide valuable insights into the effectiveness of the proposed changes and to guide the future development of the system.

Section 2: Literature Review and Background Information

This section provides a comprehensive overview of the existing literature and background information related to the study. It begins with a discussion of the current state of the art in the field, highlighting the key findings and challenges. The next part of the section focuses on the specific aspects of the study that are relevant to the proposed changes. This includes a review of the mathematical models and the experimental methods used in previous studies. The section concludes with a summary of the key findings and a discussion of the implications for the current study. The literature review is intended to provide a solid foundation for the study and to identify the gaps in the existing knowledge that the study aims to address.

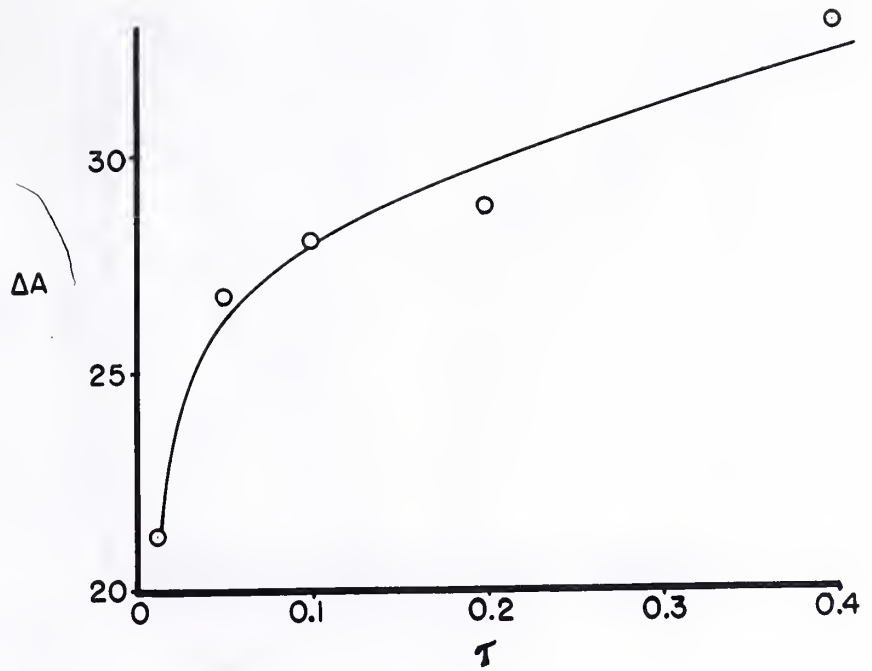


Fig. 8: Dependency on impulse duration. Data from experiment in which impulse duration varied; impulse amplitude constant at 0.5.

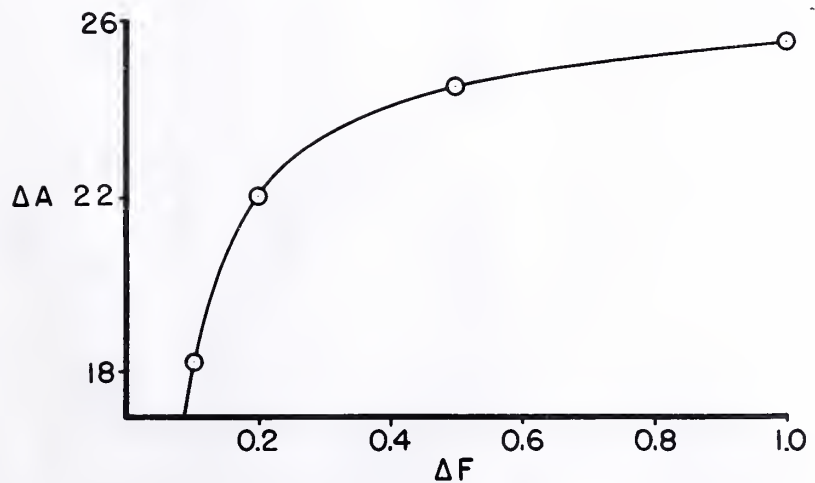


Fig. 9. Dependency on impulse amplitude. Data from experiment in which impulse amplitude varied; impulse duration constant at 0.05 secs.

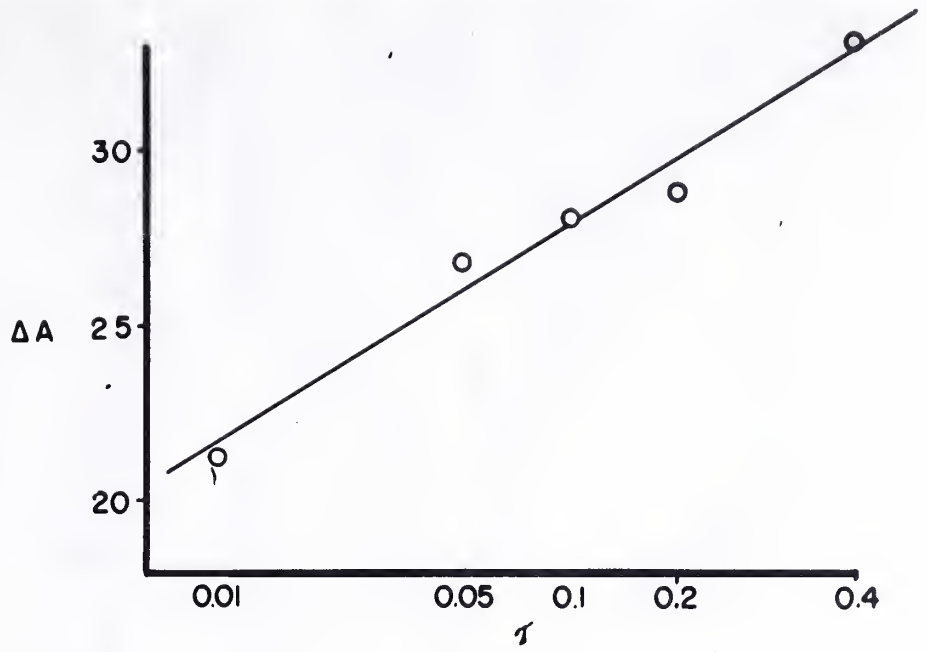


Fig. 10. Log plot of duration data of Fig. 8.

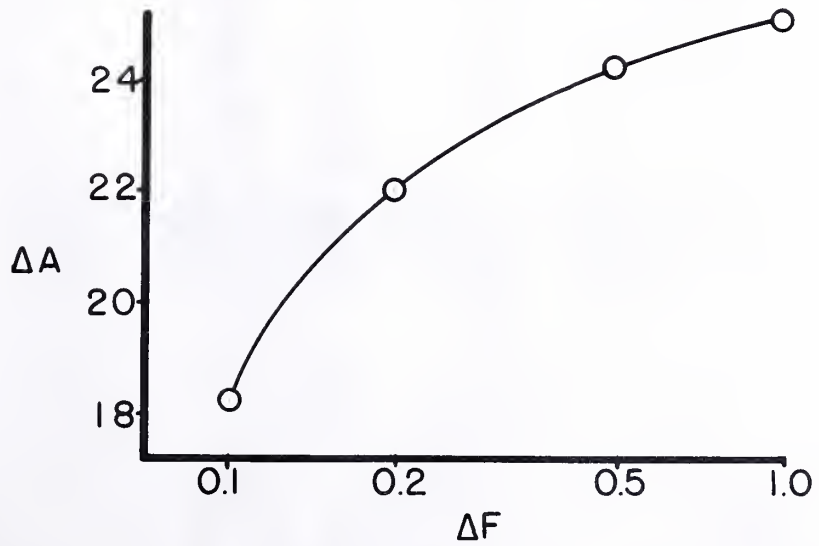


Fig. 11. Log plot of amplitude data of Fig. 9.

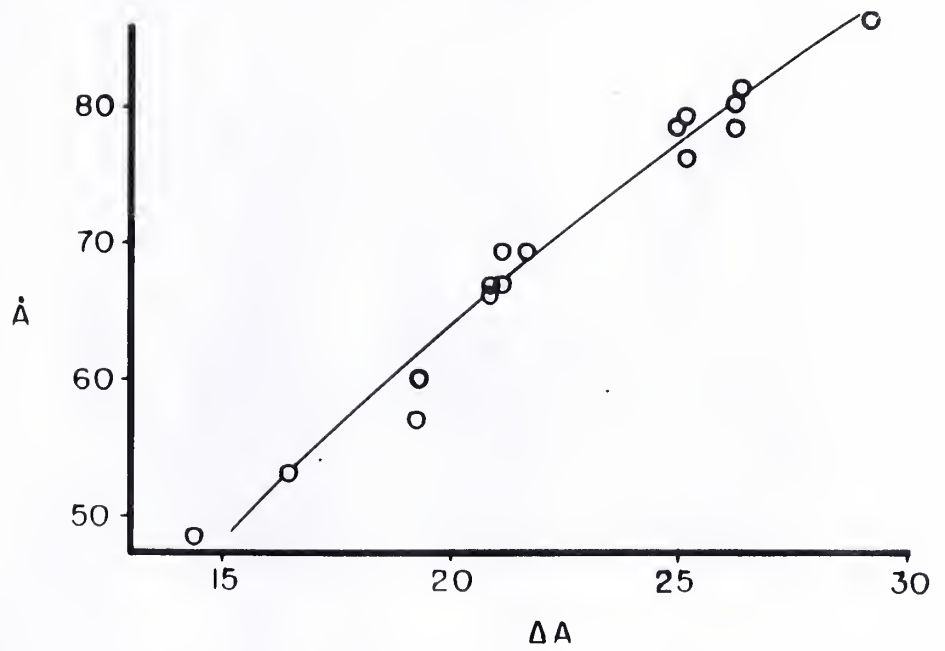


Fig. 12. Maximum rate of area change vs. maximum response amplitude. Relationship is relatively linear.

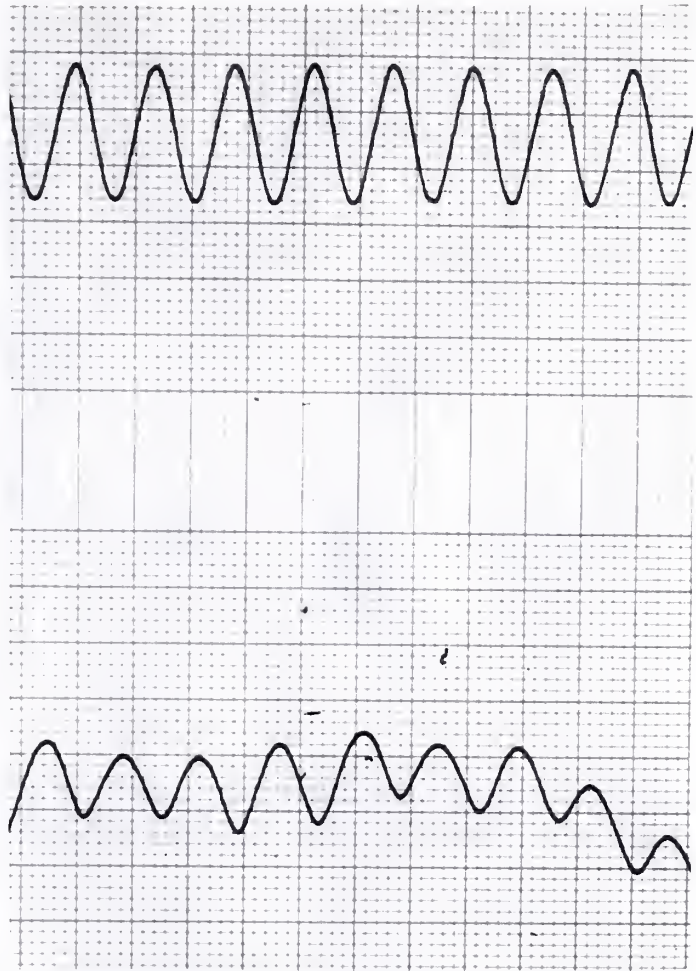


Fig. 13. Sample of sinusoidal response data. Upper curve gives input variation of light level around a mean. Lower curve shows response. Frequency is 1.4 cps.

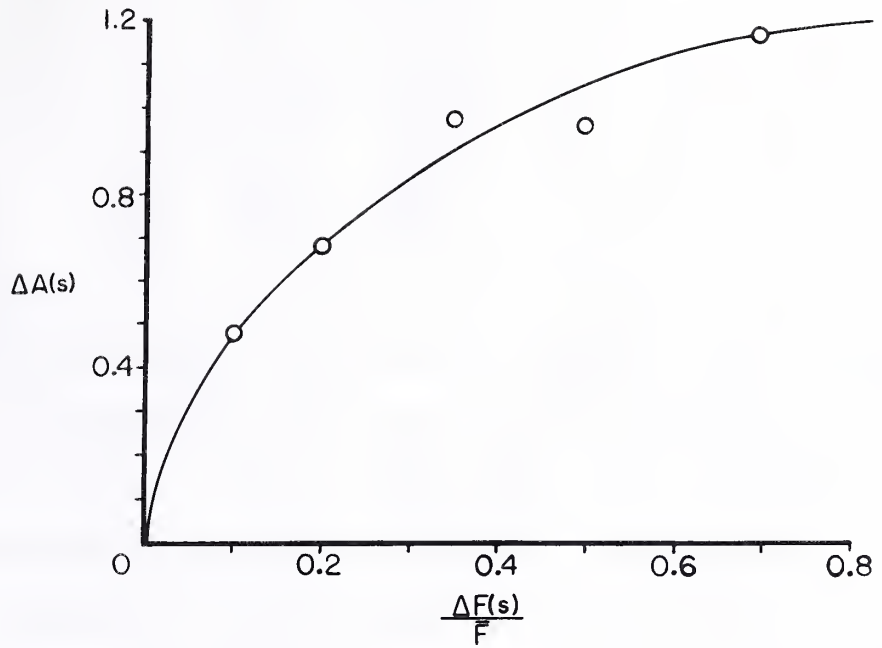


Fig. 14. Sinusoidal amplitude dependency on percentage modulation of light. Curve extrapolated to origin.

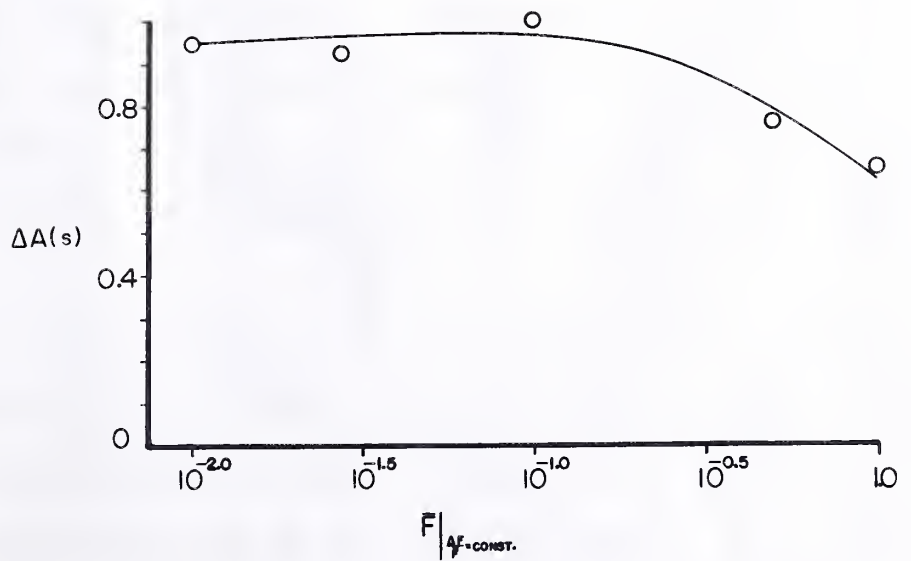


Fig. 15. Sinusoidal amplitude dependency on mean light level. Shows relatively little dependence.

CHAPTER VII

DISCUSSION

Sinusoidal Data:

The problem which the sinusoidal experiments were designed to attack is the determination of the nature of the dependency of output on the driving function. If the output were primarily dependent on the absolute amplitude of the input, one would expect large changes in output for a ten fold change in mean light level keeping percentage modulation constant. On the contrary, it has been shown that the output did not increase with an increase in mean level, but in fact probably fell off at higher levels. On the other hand a change in the percentage modulation produced a corresponding change in the same direction in the output. Since zero percent modulation would produce zero output, the output vs. input percent modulation curve shown in Fig. 14, p. 40, crosses the positive abscissa. For purposes of curve fitting we have taken the logical step of drawing the curve through the origin. It will be noted that this relationship is non-linear.

In summary, then, the significance of the results of these experiments may be simply stated: Within the range investigated, the significant driving function is not the absolute amplitude but rather the percentage amplitude change of the input sinusoid.

Pulse data: general discussion

Since the pupil system has already been considered from the standpoint of linear analysis with regard to response in the frequency

domain, it would be well to begin our evaluation of the pulse experiments in terms of comparable linear systems suggested by those investigations. The weight of this suggestion is pressed upon us because linear theory demands a one to one correspondence between the two domains, i.e. suitable time data and frequency data will both completely describe a system and results from one method transform into that of the other. Stark and Sherman suggested that their data might be interpreted as indicating a three lag system, and for their analysis they called each lag approximately equal to 0.1 sec. We will therefore discuss the response of two, three, and four lag linear systems to single pulse inputs.

Systems which may be represented by first order differential equations, or single lag systems, respond to a pulse by an exponential rise through the duration of the pulse with an exponential fall immediately following. The data on the present system had a peak of response well after the cessation of the impulse, and there is also a significant foot in the rising phase. Single lag systems can therefore be excluded from consideration.

Curves in time of multilag systems show a gross similarity but differs on closer inspection. Increasing order increases the extent of the foot of the rising phase and the rapidity of descent of the falling phase for a given duration to peak. These characteristic differences are illustrated in the superimposed plots of two, three and four lag systems with equal time constants shown in Fig. 16. Time constants and gains have been adjusted to give equal peaks of response. The scale of the coordinates is arbitrary.

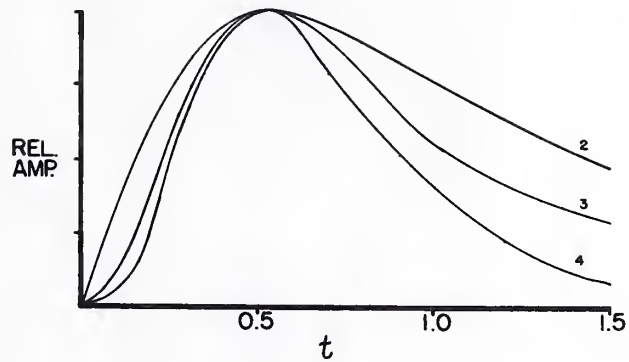


Fig. 16. Pulse responses of ideal 2, 3, and 4 lag systems. Gain factor and time constant adjusted to make peaks coincide.

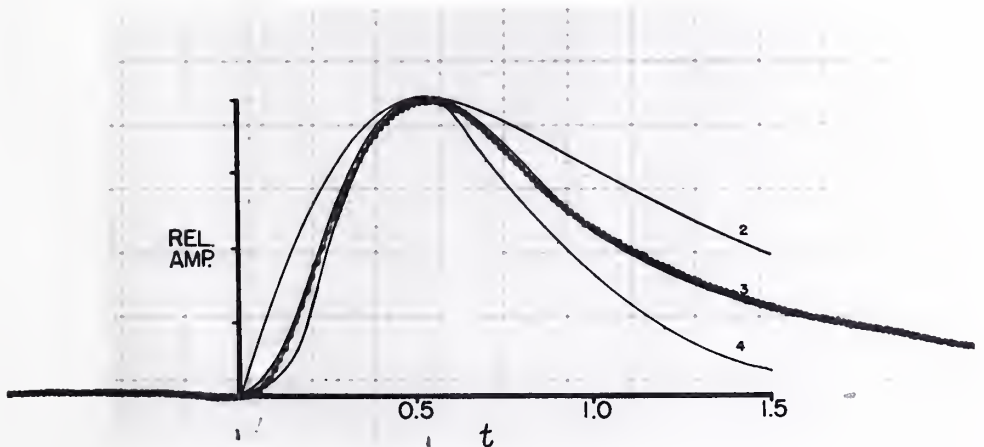


Fig. 17. Representative pupil response compared with ideal lag systems. Input pulse duration was 0.05 secs.; amplitude was 0.2 units.

In Fig. 17 a reproduction of a response of the pupil system is compared with the ideal responses of Fig. 16. Peak responses have been adjusted to coincide. It is evident that the pupil system closely resembles a third order system, in excellent correspondence with the hypothesis derived from frequency domain studies.

Critical quantitative characteristics:

A fundamental notion in linear analysis is the impulse response of a system. The impulse input is a pulse, the duration of which has been reduced to an infinitesimal interval and the magnitude increased infinitely in such a way that the energy content of the function equals one. In practice the impulse function may be approximated by pulses with durations less by an order of magnitude than the time constant of the system. Magnitude of response of linear systems to such inputs is proportional to energy content (amplitude x duration) of the pulse and response duration to peak is a minimum for a given system. Pulses of longer duration produce responses which fall away from the energy-magnitude proportionality and in which the duration increases beyond that seen for impulses. For long pulse durations the response amplitude asymptotically approaches that seen in responses to a step while the duration to peak approaches the duration of the pulse. These relationships are diagrammed schematically for a multilag system in Figs. 18 and 19.

Impulse time to peak is closely related to the time constants of the system. In a system with equal lags the relationship is simply

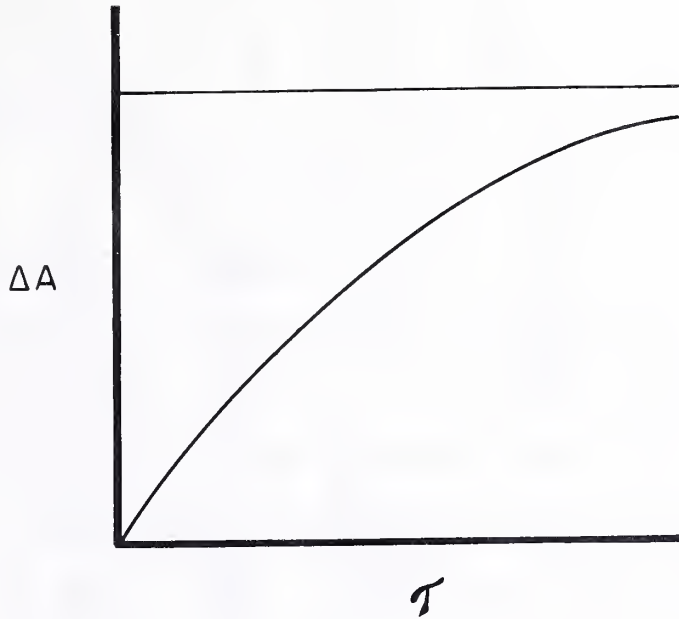


Fig. 18. Maximum amplitude vs. input pulse duration.
Diagrammatic representation of arbitrary physical system.
Curve asymptotically approaches step response amplitude.

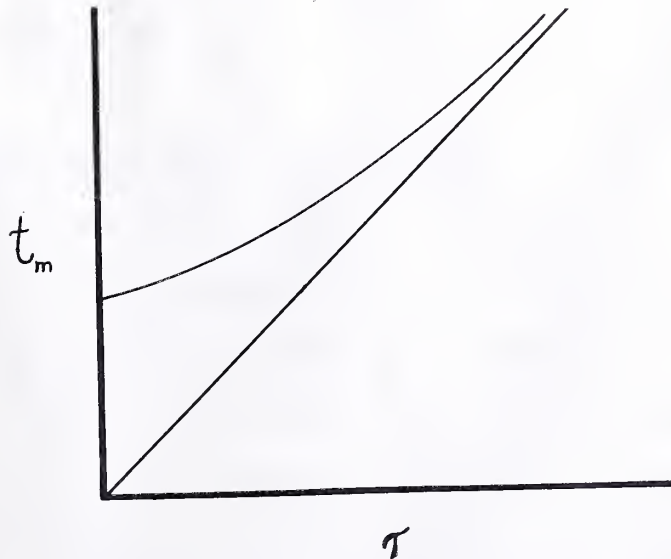


Fig. 19. Duration to peak response vs. input pulse duration.
Diagrammatic representation of arbitrary physical system.
Curve asymptotically approaches duration of pulse.

the proportionality

$$t_m = \frac{T}{n-1}$$

where n is the order of the system.

Comparison of the pupil system to two, three and four lag systems is illustrated in Figs. 20 and 21, in which experimental points are represented by circles. Maximum response height increases only gradually on a plateau with increasing duration and only at the shortest duration pulse is there an indication of a break from the high maintained value. Experimental values for duration to peak fall below the curve which represents this relationship in the linear systems.

It is important to note that the extrapolated value of the durations to peak is about 0.50 secs. If the pupil system had three equal lags, this would indicate that the values of the time constants would be 0.25 secs.

Response as a function of input pulse amplitude

Fig. 9, p. 36, indicates that amplitude is a non-linear function of the input. In accordance with the Weber-Fechner law response of sensory systems frequently is compared to the log of the input amplitude. As seen in the log plot of the data on this system illustrated in Fig. 11, the relationship is still not a proportionality. As was mentioned in Chapter V [Methods], though, there was a small minimum light level present on which the pulses were superimposed, and this might have changed the level of retinal adaptation. Response to small pulses would be affected more than that to large pulses resulting

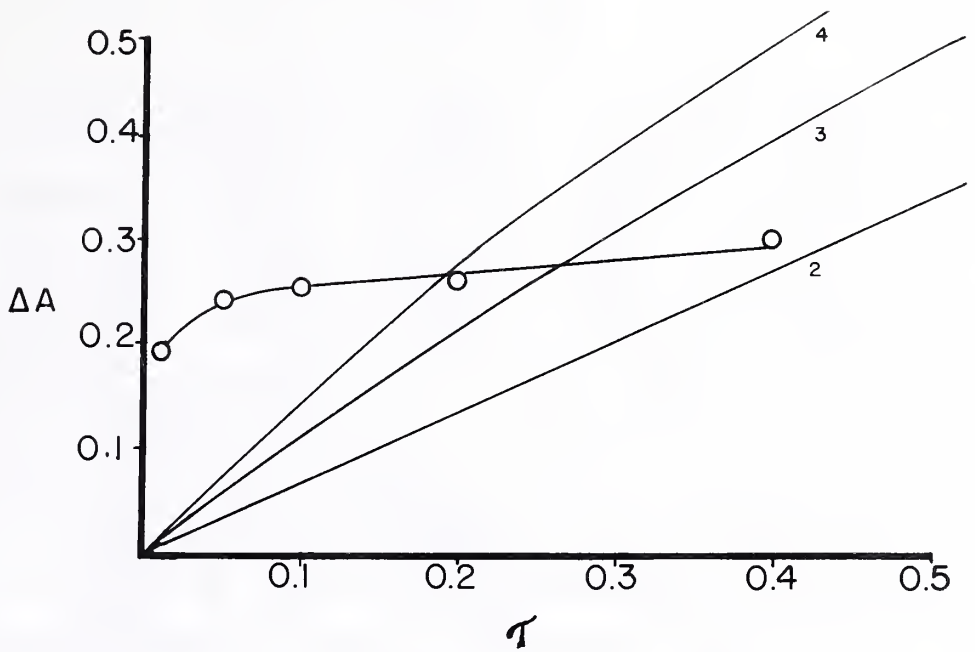


Fig. 20. Amplitude vs. pulse duration in pupil and ideal 2, 3, and 4 lag systems. Gain of pupil system arbitrary. Time constants of lag systems are equal and values obtained from duration to peak data, Fig. 21.

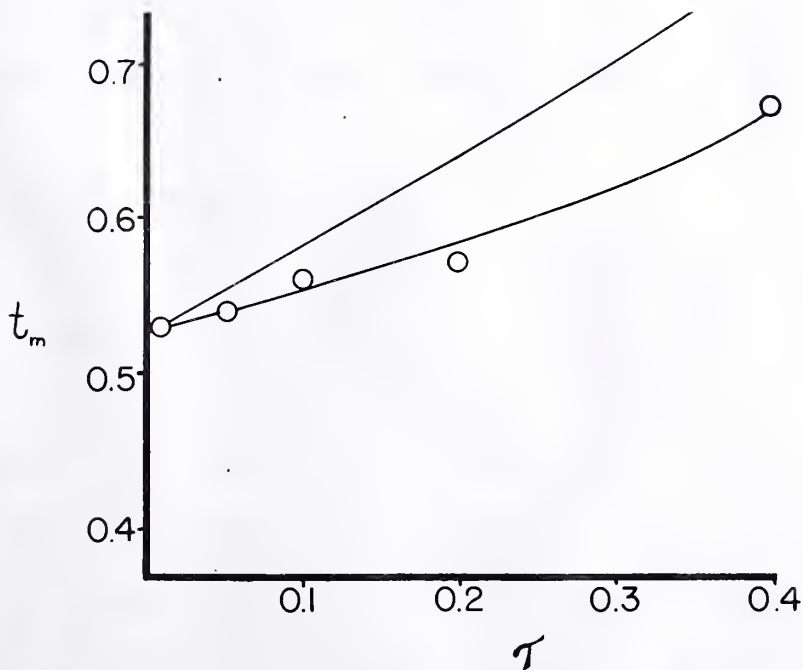


Fig. 21. Duration to peak vs. pulse duration in pupil and ideal 2, 3, and 4 lag systems. Pupil system represented by lower curve through data. Time constants of ideal systems are equal and adjusted to give impulse duration equal to that of the pupil system.

in lower amplitudes at those values. Thus, system response might well be proportional to the log input in this range of operation.

An argument against an hypothesis of mechanical range limiting in the motor system producing amplitude saturation, similar to that used by van der Tweel, is based on the maximum rate of response vs. amplitude of response relationship. If there were amplitude saturation, one would expect a maximum response rate vs. amplitude curve as illustrated in Fig. 22. This is to be compared with the relationship in a velocity saturation system illustrated in Fig. 23. The curve of experimental values shown in Fig. 12, p. 38, clearly does not have an upward concavity, and in fact might have a slight downward concavity suggesting velocity saturation. This is of interest, since Stark (1961) has postulated velocity saturation in this system to account for data derived in a totally different way. The evidence is therefore against mechanical range limiting in this operating range.

Critique of the linear lag hypothesis

The form of the response of the pupil system to pulses fits very well with the hypothesis that the system consists of three equal lag elements as the primary response shaping parameters. A log-like amplitude operator could well be incorporated into such a scheme as long as it came earlier in the system than the frequency dependent elements, required by the argument presented by Selin. The present evidence would indicate that the time constants were equal to 0.25 secs. This value lies at the upper extreme to the range for the time constant

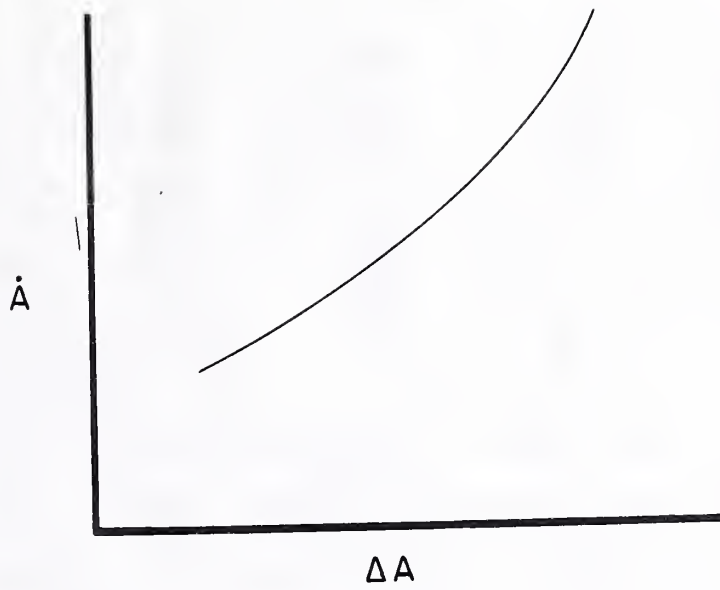


Fig. 22. Maximum rate vs. maximum amplitude relationship in system with mechanical limit saturation.

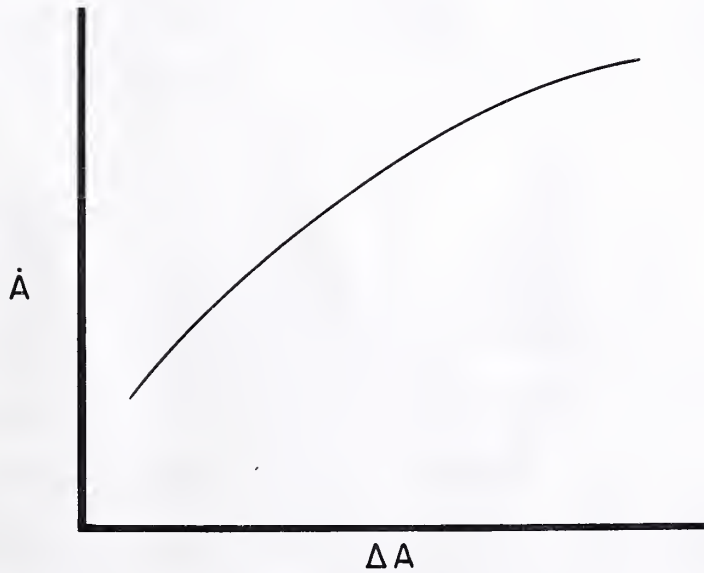


Fig. 23. Maximum rate vs. maximum amplitude relationship in system with velocity saturation.

suggested by Stark and Sherman, but it would be an even more suitable value for our own amplitude vs. frequency data. From the work of Stark and Baker (1958), who demonstrated a large shift in frequency of natural oscillation following the application of drugs to the cornea, the proposed system would most likely have the major lag components at the periphery.

The data on the maximum amplitude and the duration to peak as functions of pulse duration, though, would indicate that other processes are in operation not accounted for by this hypothesis. While it is not necessary to discard the above concepts in the light of this evidence, certain modifications are required to make the theory more complete. Although the present experimental work presents insufficient data to justify construction of an elaborate theory, the remainder of this chapter will discuss what might be a fruitful point of view towards this system, accounting for the latter data and yet preserve the afore mentioned hypothesis.

A proposed mechanism:

If energy is taken to be the significant driving function, the experimentally derived relationship of amplitude vs. pulse duration makes evident that short pulse durations are favored over long durations in the response of the system. Such relationships have been well studied and documented in the physiology of sensory elements (See the Handbook of Physiology, section of neurophysiology, V. I). Classically, a receptor system initially responds to a stimulus with high frequency firing which decreases with time to either a low maintained value or to

zero. Hartline and Grahm (1932) showed this process to take place in single receptor elements in the arthropod eye. Riggs et al (1953) have demonstrated the adaptation process in the human eye by maintaining the projection of a stimulus on one set of receptors using an optical arrangement. Hartline et al (1959, review) have analyzed a process of adaptation in the eye of *Limulus* which is accounted for solely by neuronal interaction mechanisms. Similar physiological arrangements exist in the mammalian eye which could result in similar properties.

In the light of the experimental evidence and these physiological mechanisms, which might well be operating in this system, one can conceive of an operator early in the system such as that depicted in Fig. 24. Short duration impulses would be to a large part passed but the later phases of long duration pulses would be greatly attenuated. By proper adjustment of the parameters, the convolution of such a function with the proposed lag system could duplicate the characteristics of maximum amplitude vs. pulse duration curve. The presence of such an operator would also explain the experimental duration to peak vs. pulse duration curve. With such an operator, in principle well within the confines of neurophysiological mechanisms, combined with the concept of a system of three equal lags, the data here presented can be well explained.

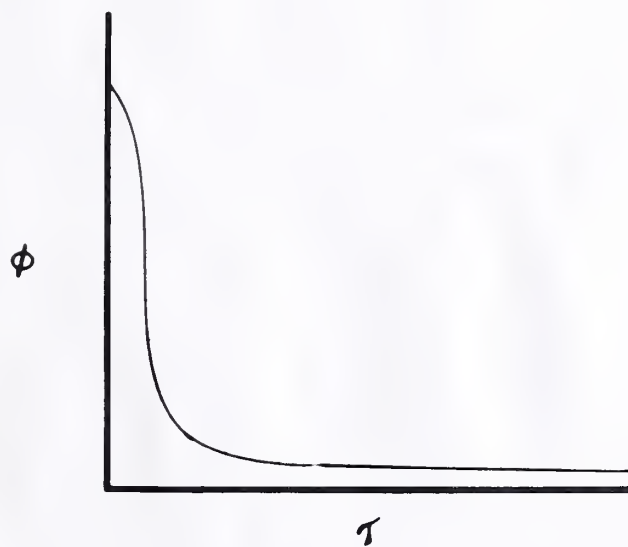


Fig. 24. Possible input operator. General form of hypothesized operator which could account for pulse data.

CHAPTER VIII

CONCLUSIONS

The problem in question has been to investigate the functional dependencies of pupil area on light flux at the plane of the retina. Experiments in two different modes of system operation have given us separate pieces of information concerning this relationship. Results of the sinusoidal experiments have not been theoretically explored. In the discussion of the pulse experiments the view point that the response of the system is primarily shaped by a multilag network is modified to generate a relationship more consistent with the present data. While the idea of the time dependent input function accords with neurophysiological concepts, no attempt has been made to formalize this relationship. The present study only hints at the form of the function and does not offer enough data for a good analysis. For these reasons the hypothesis has only been touched upon, and no further investigation has been made of the consequences.

Specifically, an attempt has not been made to correlate the pulse response with amplitude dependent sinusoidal response characteristics. Yet, as previously mentioned, Tyler has pointed out that the rate of rise of the response to a step function is not consistent with the limitations implied by the frequency response characteristics of this system. It is probable, then, that the system is operating in different states under these two different modes of stimulation. Also, Stark has demonstrated that there is hardly a break in the amplitude of response to a sine wave input when the mean level is cut by an order of

magnitude. This implies that the accommodation process accounting for this phenomenon is rapid. These two observations make reasonable an identification of the dependency of sinusoidal output on percentage light change and the hypothesized function in the impulse analysis. Much more work, though, needs to be done with the pulse experiments before such a relationship can be established. In particular, a greater range of pulse durations must be explored, as well as the effect of light adaptation on pulse response.

In the final analysis the goal of these studies is to obtain the complete functional relationship between light in and area out. Input-output analysis, along with ideas of basic physiological mechanisms, has lead to an increased understanding of these relationships, or at least has presented some rational formulations. It is not to be expected that systems analysis alone will lay open the fundamental mechanisms of the pupil system. Indeed, such techniques are geared rather to illucidate functional forms of response and in this capacity tests hypotheses and makes suggestion as to the nature of the fundamental mechanisms. Thus used, this method has much more to offer in assisting the investigation of complicated signal flow systems.

CHAPTER IX

SUMMARY

- 1) The advantages of using the pupil system as a model for a study of neurological reflex are presented.
- 2) Relevant anatomy and recent physiological investigation is reviewed.
- 3) The point of view of systems analysis is developed, and illustration made of use to which it has been put in study of the pupil system.
- 4) The experimental methods of the present study are reviewed, and designs for experiments clarifying the dependency of the response on input parameters for the sinusoidal and pulse modes of stimulation are outlined.
- 5) Results of the sinusoidal experiments indicate that amplitude of response is primarily dependent on percentage light change rather than the absolute value of light change.
- 6) Results of the pulse experiments demonstrate that the form of the response fits very well the time curve of response of a third order physical system.
- 7) The dependency of response on pulse amplitude indicates that there is probably a log operator early in the signal flow path. A linear maximum rate vs. maximum amplitude relationship supports the hypothesis that there is minimal mechanical limiting of the iris in this range of operation.
- 8) The characteristics of second, third and fourth order linear systems are reviewed, and it is shown that the pupil system cannot be directly compared to a network of simple lags. An hypothesis is presented to account for this discrepancy.

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